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A NON-SYNONYMOUS SNP IN GENE ASSOCIATED WITH SUSCEPTIBILITY TO SYMPTOMATIC OSTEOARTHRITIS

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Purpose: To search for new major symptomatic osteoarthritis (OA) susceptibility loci.
Methods: A genome wide linkage scan was performed of 403 microsatellite markers with an average spacing of 10 cM in the ongoing GARP study, which consists of 179 Caucasian sibling pairs and four trios of Dutch origin affected predominantly by symptomatic OA at multiple sites. A chromosomal region with linkage was further investigated by combined linkage association to localize the susceptibility gene. Replication by association was performed in the UK study consiting of 360 knee replacements and 1106 hip replacements versus 714 controls and in the 1712 females of the Rotterdam population based study.
Results: Suggested evidence for linkage in The GARP study was observed on chromosome 14q32.11 (LOD = 3.03, P = 0.000187). The location of the linkage peak revealed three candidate genes. Combined linkage association revealed a non synonymous coding variant which explained part of the linkage (P = 0.006). Subsequent replication in two independent OA studies revealed a common haplotype, exclusively containing the non synonymous SNP which showed significant recessive association (OR 1.71, 95% CI 1.33-2.19, $P = 2.6 \times 10^{-5}$) in females with symptomatic hip OA.
Conclusions: Evidence for a potentially new OA susceptibility gene was found.

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THE INCREASED FREQUENCY OF IL-1RN*2 ALLELE OF THE INTERLEUKIN-1 RECEPTOR ANTAGONIST GENE IN CZECH PATIENTS WITH EROSIVE HAND OSTEOARTHRITIS

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Purpose: Hand osteoarthritis (hOA) represents one particular form of OA and it is associated with degeneration of hand and finger articular cartilage. Since one of the major mediator of cartilage desintegration is interleukin-1 (IL-1) in general, interleukin-1 receptor antagonist (IL-1RA) might act as a natural inhibitor of IL-1 induced cartilage breakdown. The association of IL-1RN gene polymorphisms and OA was previously shown. The aim of the study was to test the VNTR polymorphism in the second intron of IL-1RN gene as the putative factor contributing to development of erosive hand OA.
Methods: PCR using the primers flanking VNTR region containing variable number of 86 bp tandem repeat was employed to test the hypothesis. The patients with clinically symptomatic primary hOA were diagnosed according to ACR criteria.
Results: The total of 74 patients hOA was analyzed. Based on radiological progression they were divided into two groups, patients with erosive form of the disease (48/74; 64.9%) and those showing no erosions (26/74; 35.1%). The frequency and carriage rates of allele IL-1RN*2 was higher (statistically non-significant) in patients with erosive form of hand OA in comparison to patients without erosions (10.4% vs. 7.7% for allele frequency; and 14.6% vs. 7.7% for the carriage rate).
Conclusions: These results might suggest that IL-1RN*2 allele may represent a factor influencing the severity and course of hOA. However, it is necessary to include additional patients into the study to address this question.
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Imaging

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SIZE OF SUBCHONDRAL BONE AREAS OF THE KNEE AS A FUNCTION OF ALIGNMENT - A LONGITUDINAL QUANTITATIVE MRI-BASED ANALYSIS

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Purpose: To determine the ratio of the size of medial versus lateral subchondral bone areas in the knees of participants with varus, valgus and neutral knee alignment, and to analyze longitudinal changes in subchondral bone areas over 2 years in the same cohort.
Methods: A community-recruited cohort with moderate radiographic knee OA (n = 174; age 66 $\pm$ 11 y.; BMI 30.2 $\pm$ 6.1, 76% women) had alignment measurement by full limb x-ray: 74 had neutral alignment (-2° to +2° deviation from the biomechanical knee axis), 57 had varus (> +2°), and 43 valgus malalignment (< -2°). A coronal FLASHwe sequence (1.5 x 0.31 x 0.31 mm^3 resolution) was acquired at baseline and 26.6 $\pm$ 5.4 months later using 1.5 and 3.0T scanners. Segmentation of the total subchondral bone area (tAB) of the medial and lateral tibia (MT/LT) and of the medial and lateral weight-bearing central femur (cMF/cLF) was performed using proprietary software (Chondrometrics GmbH, Ainring, Germany). The segmentation included areas denuded of cartilage in cases where denuded areas were present, but excluded osteophytes in all cases. Baseline and follow up scans were processed in parallel with blinding to acquisition order. All segmentations were quality controlled by one expert reader.
Results: The average ratio of the size of the subchondral bone area (tAB) between the medial and lateral tibia was 1.20 $\pm$ 0.15. The ratio was significantly higher ($p<0.001$) in participants with varus malignment (1.28 $\pm$ 0.17) compared with neutral knees (1.18 $\pm$ 0.12), and it was significantly smaller ($p<0.05$) in the participants with valgus malignment (1.13 $\pm$ 0.13). The average ratio of cMF versus cLF was 0.94 $\pm$ 0.09. The ratio in varus participants (0.97 $\pm$ 0.11) tended to be higher than in neutral knees (0.94 $\pm$ 0.08) and the ratio in valgus knees (0.91 $\pm$ 0.07) lower than in neutral knees. The difference between varus and valgus knees was significant ($p<0.01$). The annualized increase in tAB over 27 months was 0.13% ($p<0.05$) per year in MT, 0.19% ($p<0.05$) in LT, 0.26% ($p<0.05$) in cMF and 0.06% (not significant) in cLF. The longitudinal change in MT, in LT, and in the ratio between MT and LT was not significantly different between varus, valgus and neutral knees. The increase in cLF, however, was significantly higher ($p<0.05$) in valgus participants (0.32%) compared with neutral (-0.14%) and varus knees (0.12%), and the increase in cMF was significantly higher ($p<0.05$) in varus knees (0.67%) than in neutral (0.06%) and valgus knees (0.03%).
Conclusions: The ratio of the size of medial versus lateral subchondral bone areas was significantly different in OA participants with varus, valgus and neutral knee alignment, with the tAB being significantly larger in the mechanically more stressed compart-